```
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LOGINID:sssptal201txs
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1  Feb  2  Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jul  8  Important Derwent Announcement about CPI Changes to
                  CPI Subscriber Indexing in 1999 - REVISED
 NEWS  3  Jun 28  REGISTRY Updated Daily
 NEWS  4  Jul  7  PATOSWO Coverage Extended to 1978 through 1982
                  Backfile
 NEWS  5  Jul  7  COMPENDEX Accession Number Change
 NEWS  6  Jul 13  Expanded Coverage of US Patents
 NEWS  7  Jul 14  ENERGY Accession Number Change
 NEWS  8  Jul 18  MEDLINE Now Searchable from 1960 to Date
 NEWS  9  Jul 21  INSPEC Accession Number Display Changes

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:48:51 ON 23 JUL 1999

=> file reg

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    0.15       0.15

FILE 'REGISTRY' ENTERED AT 11:49:00 ON 23 JUL 1999
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STRUCTURE FILE UPDATES:   23 JUL  99  HIGHEST RN 228731-40-6
DICTIONARY FILE UPDATES:  23 JUL  99  HIGHEST RN 228731-40-6
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USCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Uploading 9077718.str

L1      STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 11:49:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     13 TO ITERATE
100.0% PROCESSED      13 ITERATIONS                                 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           44 TO      476
PROJECTED ANSWERS:               2 TO      124

L2            2 SEA SSS SAM L1

=>
Uploading C9077718.str

L3      STRUCTURE UPLOADED

=> s l3

SAMPLE SEARCH INITIATED 11:50:31 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   1835 TO ITERATE
 54.5% PROCESSED    1000 ITERATIONS                                50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        34133 TO    39267
PROJECTED ANSWERS:            5886 TO     8132

L4           50 SEA SSS SAM L3

=> s l1 sub=l3 sam

L3 MAY NOT BE USED HERE
The L-number must have been created by a search in this file.  To see
all L-numbers defined in this session, enter DISPLAY HISTORY at an
arrow prompt (=>).  For additional information on subset searching in
this file, enter HELP SUBSET.
ENTER SUBSET L# OR (END):end

SEARCH ENDED BY USER

=> help subset


 Subset searching is available for structure searches in the REGISTRY
 File.  A subset search may be performed on any answer set created in
 this file.  Structure search answer sets must have been created
 after April 15, 1989.
```

SAMPLE, FULL, or RANGE must be specified as the subset search scope. There is no default subset search scope.

SSS, CSS, FAM, or EXA may be specified as the subset search type. SSS is the default subset search type.

Example:

=> SEARCH L5 SUBSET=L3 SAM SSS

The same query limitations that apply to non-subset searches in this file also apply to subset searches. The search limits for a subset search are the same as those for an online non-subset search of the same type and scope.

Additional information on subset searching may be found in the following help messages:

```
HELP SEARCH SUBSET - Information on how to perform a subset
                     search
HELP COST          - Fees for subset searches
HELP SLIMIT        - Structure search limits in this file
```

```
-> s l1 ful

FULL SEARCH INITIATED 11:53:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    171 TO ITERATE
100.0% PROCESSED     171 ITERATIONS                          29 ANSWERS
SEARCH TIME: 00.00.01

L5            29 SEA SSS FUL L1

-> s l3 ful

FULL SEARCH INITIATED 11:53:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  36343 TO ITERATE
100.0% PROCESSED   36343 ITERATIONS                      8067 ANSWERS
SEARCH TIME: 00.00.02

L6          8067 SEA SSS FUL L3

-> s l5 sub=l6

ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):ful

FULL SUBSET SEARCH INITIATED 11:54:04 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -     10 TO ITERATE
100.0% PROCESSED      10 ITERATIONS                         5 ANSWERS
SEARCH TIME: 00.00.01

L7             5 SEA SUB=L6 SSS FUL L1

-> d l7 hitstr abs ibib 1-5

'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
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fields or predefined formats. The predefined substance formats are: (RN CAS Registry Number)

RN - RN
CAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS --ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

The ALL format gives FIDE BIB ABS IND, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

> file caplus uspatful

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	273.00	273.15

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FILE 'USPATFULL' ENTERED AT 11:54:54 ON 23 JUL 1999

-> s l7

L8 18 L7

=> dup rem l8

PROCESSING COMPLETED FOR L8
L9 9 DUP REM L8 (1 DUPLICATE REMOVED)

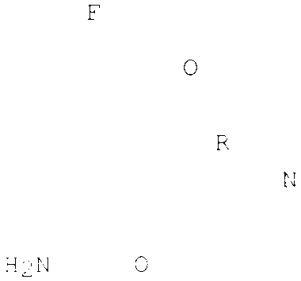
=> d l9 hitstr abs ibib 1-9

L9 ANSWER 1 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, Nad 299
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. monoamine oxidase inhibitor as antidepressant)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

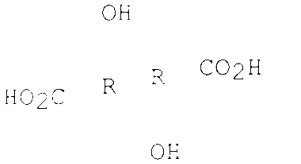
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB Pharmaceutical compns. contain a monoamine oxidase inhibitor, a 5-HT1A presynaptic antagonist and a 5-HT1A agonist as combination product to be used simultaneously, sep. or spread over time for treating different terms

st depression. Antidepressant efficacy of a combination of 3 mg/kg befloxatone i.p., 1 mg/kg pindolol i.p., and 0.3 mg/kg buspirone i.p. was studied in rats.

ACCESSION NUMBER: 1999:219988 CAPLUS
DOCUMENT NUMBER: 130:247053
TITLE: Pharmaceutical compositions containing a monoamine oxidase inhibitor as antidepressant
INVENTOR(S): Depoortere, Henri
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

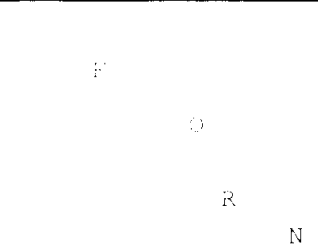
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913879	A1	19990325	WO 1998-FR1929	19980910
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2768338	A1	19990319	FR 1997-11545	19970917
AU 9890819	A1	19990405	AU 1998-90819	19980910
PRIORITY APPLN. INFO.:			FR 1997-11545	19970917
			WO 1998-FR1929	19980910

L9 ANSWER 2 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, (R)-3-N,N-Dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide (2R,3R)-tartrate
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT1A antagonist; prepn. and/or therapeutic combination of selective 5-HT1A antagonists with selective h5-HT1B antagonists or partial agonists)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

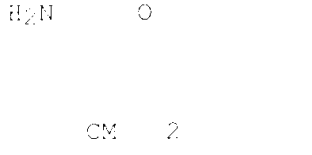
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a combination of a first component (a) which is a selective 5-HT1A receptor antagonist I [wherein R1 = Pr or cyclobutyl, R2 = iso-Pr, tert-Bu, cyclobutyl, cyclopentyl, or cyclohexyl; R3 = H and R4 = H or Me], being in the (R)-enantiomer form, with a second component (b) which is a selective h5-HT1B antagonist or partial agonist II [wherein X = CH2 or O; Y = CONH or NHCO; R1 = H, C1-6 alkyl, or C3-6 cycloalkyl; R2 = H, C1-6 alkyl, C1-6 alkoxy, or halo; R3 = morpholino, morpholinocarbonyl, 4-oxopiperidino, CF3, or CONR4R5; R4, R5 = H or C1-4 alkyl], as a racemate or either enantiomer, with said components (a) and (b) being in the form of free bases, solvates, or pharmaceutically acceptable salts. The invention also relates to their prepn., combination pharmaceutical formulations, use, a method of treating affective disorders such as depression, anxiety, and OCD using the combinations, as well as a kit contg. the combinations. The combinations of the invention may afford a new route to faster onset of action in antidepressant therapy. For instance, amidation of 4-morpholinobenzoic acid with (R)-2-amino-5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydronaphthalene using 1,1'-carbonyldiimidazole in DMF gave 73% III. Using III as the h5-HT1B antagonist, and benzopyrancarboxamide deriv. IV (tartrate salt) as the 5-HT1A antagonist, a synergistic increase in 5-HT turnover was obtained in

4 brain regions of guinea pigs, as compared with compd. III alone.

ACCESSION NUMBER: 1999:219985 CAPLUS
DOCUMENT NUMBER: 130:252381
TITLE: A combination of a selective 5-HT1A antagonist [benzopyran derivative] and a selective h5-HT1B antagonist or partial agonist [piperazinonaphthalene or -benzopyran derivative] for antidepressant therapy
INVENTOR(S): Berg, Stefan; Ross, Svante; Thorberg, Seth-Olov
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913876	A1	19990325	WO 1998-SE1600	19980909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9891929	A1	19990405	AU 1998-91929	19980909
PRIORITY APPLN. INFO.:			SE 1997-3374	19970918
			WO 1998-SE1600	19980909

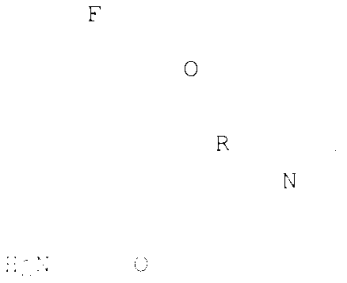
OTHER SOURCE(S): MARPAT 130:252381

L9 ANSWER 3 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, NAD-299
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(electrophysiol. comparison of 5-HT1A antagonists on dorsal raphe cell firing)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

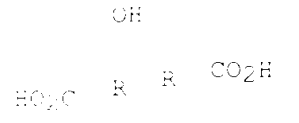
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB Single-unit recording studies were undertaken in chloral hydrate-anesthetized rats to compare the effects on dorsal raphe cell firing of several putative 5-hydroxytryptamine (HT)1A receptor antagonists, including WAY 100635 (N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-ethyl]-N-(2-pyridinyl) cyclohexanecarboxamide), p-MPPI (4-(2-methoxyphenyl)1-[2'-[N-(2''-pyridinyl)-p-iodobenzamido]ethyl]piperazine), and two newly described 5-HT1A receptor antagonists, NDL-249 [(R)-3-(N-propylamino)-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide] and NAD-299 [(R)-3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide]. Consistent with a 5-HT1A receptor antagonist profile, pretreatment with an approx. equimolar (0.02-0.03 .mu.mol/kg) i.v. dose of each compd. caused a significant rightward shift in the dose-response curve for 8-OH-DPAT [8-hydroxy-2-(di-n-propylamino)tetralin]. Antagonist potency was clearly highest for NAD-299 and WAY 100635, which caused shifts roughly 3 times greater than those for either p-MPPI or NDL-249 (ED50 for 8-OH-DPAT, 1.3 .+-. 0.3 .mu.g/kg; after NAD-299, 18.2 .+-. 1.0 .mu.g/kg; after WAY 100635, 16.9 .+-. 2.9 .mu.g/kg; after NDL-249, 6.0 .+-. 1.2 .mu.g/kg; after p-MPPI, 4.7 .+-. 1.1 .mu.g/kg). In sep. studies, each of the antagonists was administered alone in increasing cumulative doses to evaluate whether they possessed intrinsic agonist activity in this system. At doses below 0.01 .mu.mol/kg, none of the drugs altered firing by more than .+-.20% basal rates. At higher doses (>0.1 .mu.mol/kg), WAY 100635, NDL-249, and NAD-299 caused a dose-dependent suppression of dorsal raphe cell firing (ED50 = 0.6 .+-. 0.2, 0.7 .+-. 0.3, and 0.9 .+-. 0.4 .mu.mol/kg, resp.). However, the ED50 values for inhibition by these drugs were roughly 30 times higher than the doses that antagonized effects of 8-OH-DPAT. Moreover, the inhibition by all three antagonists (but not 8-OH-DPAT) was readily reversed by d-amphetamine (3.2 mg/kg i.v.), a releaser of norepinephrine, suggesting that these effects were likely due to alpha adrenergic receptor blockade rather than to 5-HT1A receptor agonism. Thus, it was concluded that WAY 100635, NAD-299, NDL-249, and p-MPPI all fulfill criteria as 5-HT1A receptor antagonists lacking intrinsic efficacy in the dorsal raphe system. The newly described compd. NAD-299 exhibits antagonist potency comparable to that of WAY 100635 in this electrophysiol. assay.

ACCESSION NUMBER: 1999:99766 CAPLUS
DOCUMENT NUMBER: 130:294350
TITLE: Electrophysiological comparison of 5-hydroxytryptamine1A receptor antagonists on dorsal raphe cell firing
AUTHOR(S): Martin, Lynn P.; Jackson, David M.; Wallsten, Carin;

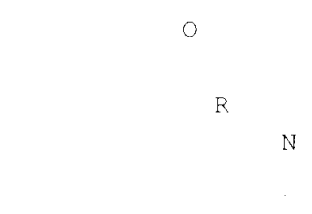
	Wasiczak, Barbara L.
[illegible] SOURCE:	Department of Pharmaceutical Sciences, Northeastern University, Boston, MA, USA
[illegible]:	J. Pharmacol. Exp. Ther. (1999), 288(2), 820-826 CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER:	American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE:	Journal
LANGUAGE:	English

L9 ANSWER 4 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, NAD-299
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(in vivo intrinsic efficacy of 5-HT1A receptor antagonists NAD-299 and WAY-100,635 and UH-301 at rat brain monoamine receptors)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

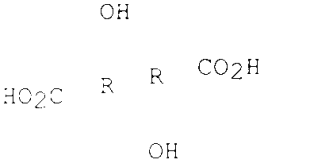
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB The receptor-mediated control of brain monoamine synthesis was used to examine the in vivo intrinsic efficacy of the 5-HT1A receptor antagonists NAD-299, S(-)-UH-301 and WAY-100,635. The rate of monoamine synthesis was

estd. by measuring the accumulation of DOPA and 5-HTP in the ventral neostriatum and the ventral hippocampus in rats pretreated with an inhibitor of cerebral arom. L-amino acid decarboxylase. S(-)-UH-301 (2.0-32.0 .mu.mol kg-1), but not WAY-100,635 (0.08-1.2 .mu.mol kg-1), produced a decreased 5-HTP accumulation in the neostriatum and in the hippocampus. The administration of NAD-299 (0.75-12.0 .mu.mol kg-1) resulted in a slight increase in neostriatal, but not hippocampal, 5-HTP accumulation. Neostriatal DOPA accumulation was decreased by S(-)-UH-301, whereas treatment with WAY-100,635 resulted in an increase. NAD-299 did not affect neostriatal DOPA levels. There were no effects by any of these agents on DOPA levels in the ventral hippocampus. It is concluded that S(-)-UH-301, but not WAY-100,635 or NAD-299, displays intrinsic efficacy at brain 5-HT1A and DA D2/3 receptors, whereas WAY-100,635 behaves as a DA D2/3 receptor antagonist. By this comparison, NAD-299 appears to be the most selective and specific 5-HT1A receptor antagonist.

ACCESSION NUMBER: 1999:45451 CAPLUS
DOCUMENT NUMBER: 130:306405
TITLE: In vivo intrinsic efficacy of the 5-HT1A receptor antagonists NAD-299, WAY-100,635 and (S)-(-)-UH-301 at rat brain monoamine receptors
AUTHOR(S): Ahlenius, Sven; Henriksson, Ingrid; Magnusson, Olle; Salmi, Peter
CORPORATE SOURCE: CNS Preclinical Research and Development, Department of Pharmacology, Astra Arcus AB, Soedertaelje, S-151 85, Swed.
SOURCE: Eur. Neuropsychopharmacol. (1999), 9(1-2), 15-19
CODEN: EURNE8; ISSN: 0924-977X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 5 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **177255-04-8P 208516-87-4P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dicyclobutylamino(fluoro)dihydrobenzopyrancarboxamide hydrogen tartrate for pharmaceuticals)
RN 177255-04-8 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1), monohydrate (9CI) (CA INDEX NAME)

CM 1

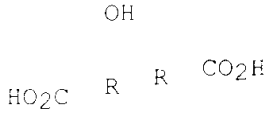
CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

Absolute stereochemistry. Rotation (-).

CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.

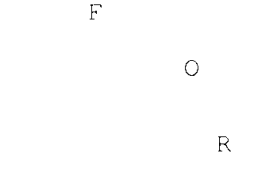


RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide,
3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-
, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

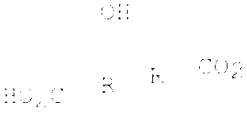
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB A new salt, (R)-3-(N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide hydrogen tartrate, particularly the (2R,3R)-tartrate salt, and most particularly the (R)-3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-car boxamide hydrogen-(2R,3R)-tartrate monohydrate, processes for the manuf. of the tartrate, the use of the tartrate salt in the manuf. of pharmaceutical formulations, and a method for the treatment of CNS disorders by using these compds. are described. Thus, the (2R,3R)-tartrate salt was prepd. by the reaction of (R)-3-(N,N)-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide with (2R,3R)-tartaric acid in 1 mL THF and 25 mL di-Et ether.

ACCESSION NUMBER: 1998:795000 CAPLUS
DOCUMENT NUMBER: 130:43350
TITLE: Preparation of (R)-3-(N,N)-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide hydrogen tartrate for pharmaceuticals
INVENTOR(S): Nyqvist, Hakan; Sohn, Daniel D.
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854166	A1	19981203	WO 1998-SE907	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9702066	A	19981201	SE 1997-2066	19970530
SE 510305	C2	19990510		
AU 9877923	A1	19981230	AU 1998-77923	19980515
PRIORITY APPLN. INFO.:			SE 1997-2066	19970530
			WO 1998-SE907	19980515

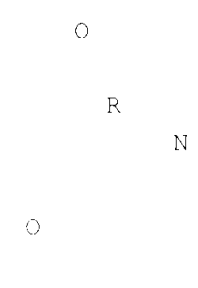
L9 ANSWER 6 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, NAD-299
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(facilitation and inhibition of male rat ejaculatory behavior by 5-HT1A and 5-HT1B receptor agonists 8-OH-DPAT and anpirtoline as evidenced by use of receptor antagonists NAD-299 and NAS-181)
RN 208516-87-4 CAPLUS

RN [(R)-1-Benzopyran-5-carboxamide,
3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-
, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

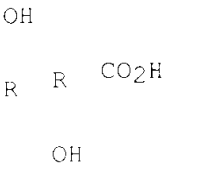
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB Ejaculatory problems and anorgasmia are well-known side-effects of the SSRI (selective serotonin reuptake inhibitor) antidepressants, and a pharmacol. induced increase in serotonergic neurotransmission inhibits ejaculatory behavior in the rat. In the present study the role of 5-HT1A and 5-HT1B receptors in the mediation of male rat ejaculatory behavior was examd. by use of selective agonists and antagonists acting at these 5-HT receptor subtypes. The 5-HT1A receptor agonist 8-OH-DPAT (0.25-4.00 .mu.mol kg-1 s.c.) produced an expected facilitation of the male rat ejaculatory behavior, and this effect was fully antagonized by pretreatment with the new selective 5-HT1A receptor antagonist (R)-3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide hydrogen (2R,3R) tartrate monohydrate (NAD-299) (1.0 .mu.mol kg-1 s.c.). NAD-299 by itself (0.75-3.00 .mu.mol kg-1 s.c.) did not affect the male rat ejaculatory behavior. The 5-HT1B receptor agonist anpirtoline (0.25-4.00 .mu.mol kg-1 s.c.) produced a dose-dependent inhibition of the male rat ejaculatory behavior, and this effect was fully antagonized by pretreatment with the 5-HT1B receptor antagonist isamoltane (16 .mu.mol kg-1 s.c.) as well as by the new and selective antagonist

R,S-)-2-(3-morpholinomethyl-2H-chromene-8-yl)oxymethylmorpholino methanesulfonate (NAS-181) (16 .mu.mol kg-1 s.c.). Isamoltane (1.0-16.0 .mu.mol kg-1 s.c.) and NAD-181 (1.0-16.0 .mu.mol kg-1 s.c.) had no, or weakly facilitatory effects on the male rat ejaculatory behavior. The non-selective 5-HT1 receptor antagonist (-)-pindolol (8 .mu.mol kg-1 s.c.), did not antagonize the inhibition produced by anpirtoline. The present results demonstrate opposite effects, facilitation and inhibition, of male rat ejaculatory behavior by stimulation of 5-HT1A and 5-HT1B receptors, resp., suggesting that the SSRI-induced inhibition of male ejaculatory dysfunction is due to 5-HT1B receptor stimulation.

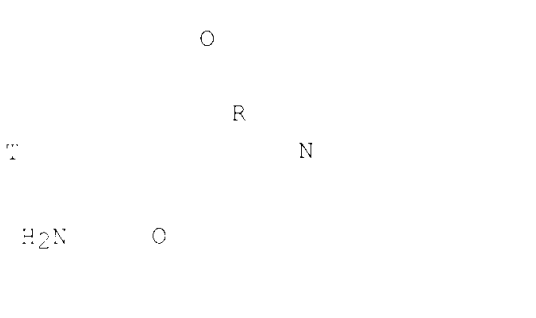
ACCESSION NUMBER: 1999:62618 CAPLUS
DOCUMENT NUMBER: 130:262483
TITLE: Facilitation and inhibition of male rat ejaculatory behavior by the respective 5-HT1A and 5-HT1B receptor agonists 8-OH-DPAT and anpirtoline, as evidenced by use of the corresponding new and selective receptor antagonists NAD-299 and NAS-181
AUTHOR(S): Hillegaart, Viveka; Ahlenius, Sven
CORPORATE SOURCE: Department of Pharmacology, Astra Arcus AB, Soedertaelje, SE-151 85, Swed.
SOURCE: Br. J. Pharmacol. (1998), 125(8), 1733-1743
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 7 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **209056-10-0**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(NAD 299 for in vivo labeling of mouse brain 5-hydroxytryptamine1A receptors)
RN 209056-10-0 CAPLUS
CN 2H-1-Benzopyran-6-t-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 209056-09-7
CMF C18 H22 F N2 O2 T

Absolute stereochemistry.

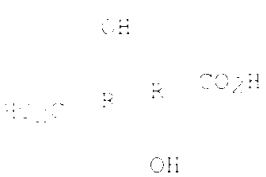


CM 2

CRN 87-69-4

CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.

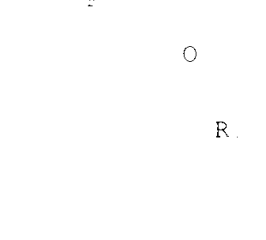


IT **208516-87-4**, NAD 299
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(NAD 299 for in vivo labeling of mouse brain 5-hydroxytryptamine1A receptors)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

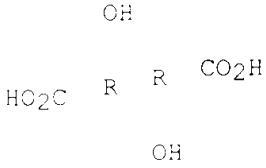
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB The in vivo labeling of 5-hydroxytryptamine (5-HT)1A receptors in the mouse brain was studied with the novel selective 5-HT1A receptor

antagonist, NAD-299
(3-[3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide hydrogen (2R,3R)-tartrate monohydrate). 3H-NAD-299 was injected in a tail vein and the radioactivity in various brain regions was detd. More than 90% of the radioactivity in hippocampus, 15 min after the injection, was intact NAD-299. At this time the amt. of 3H-NAD-299 was highest in hippocampus followed by frontal cortex, mesencephalon, hypothalamus, striatum and cerebellum. The specific accumulation of radioactivity (after subtracting cerebellum values) in frontal cortex and hippocampus was maximal 10 to 30 min after the injection and had almost disappeared after 2 h. Satn. kinetics derived Bmax (pmol/g wet wt. tissue) values of 19.6 in frontal cortex and 38.0 in hippocampus. The apparent Kd values, expressed in nmol/kg 3H-NAD-299 injected, were 12.3 in frontal cortex and 20.3 in hippocampus. The 5-HT1A receptor antagonist WAY-100,635 competitively inhibited the specific accumulation of 3H-NAD-299 and was about equipotent with unlabeled NAD-299 with ED50 values of 20-30 nmol/kg s.c. These compds. were about 10 times more potent than the 5-HT1A receptor antagonists p-MPPI and NDL-249 and 100 times more potent than (S)-UH-301. 5-HT1A receptor agonists, e.g., 8-OH-DPAT and flesinoxan and partial agonists, e.g., pindolol, buspirone and ipsapirone, had low potency in this in vivo assay. Spiperone and methiothepin inhibited the 3H-NAD-299 accumulation at 10 .mu.mol/kg s.c. The .alpha.1-adrenoceptor antagonist, prazosin, at 2 .mu.mol/kg s.c. increased significantly the specific accumulation of 3H-NAD-299. Pretreatment of the mice with the non-selective, irreversible receptor antagonist EEDQ produced a dose related long-lasting decrease in the accumulation of 3H-NAD-299. It is concluded that NAD-299 is a very suitable ligand for studies of 5-HT1A receptors in the brain in vivo.

ACCESSION NUMBER: 1998:291396 CAPLUS
DOCUMENT NUMBER: 129:63322
TITLE: In vivo labeling of the mouse brain 5-hydroxytryptamine1A receptor with the novel selective antagonist 3H-NAD-299
AUTHOR(S): Stenfors, C.; Werner, Tom; Ross, Svante B.
CORPORATE SOURCE: Preclinical R + D, Biochemical Pharmacology, Astra Arcus AB, Soedertaelje, S-151 85, Swed.
SOURCE: Naunyn-Schmiedeberg's Arch. Pharmacol. (1998), 357(5), 500-507
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 8 OF 9 CAPLUS COPYRIGHT 1999 ACS
IT **208516-87-4**, NAD 299
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(serotoninergic S1A receptor antagonists antagonism of hydroxy-DPAT-induced decrease in serotonin synthesis in different brain areas)
RN 208516-87-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (3R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2

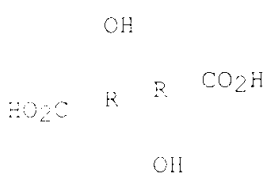
CDES 1:R

Absolute stereochemistry. Rotation (-).

CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



AB The effects of two 5-HT1A receptor antagonists, (R)-3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide hydrogen (2R,3R)-tartrate monohydrate (NAD-299) and N-(2-(1-(2-methoxyphenyl)-piperazinyl)ethyl)-N-(2-pyridinyl) cyclohexanecarboxamide trihydrochloride (WAY-100635) on the decrease in 5-hydroxytryptophan (5-HTP) accumulation evoked by (RS)-2-dipropylamino-8-hydroxy-1,2,3,4-tetrahydronaphthalene (8-OH-DPAT) in rats treated with the decarboxylase inhibitor, 3-hydroxyphenylhydrazine (NSD 1015) were studied in four rat brain regions: hippocampus, hypothalamus, striatum and frontal cortex. Dose-response studies revealed differential effects of both antagonists in the areas examd. Both antagonists were significantly more potent in antagonizing the effect of 0.30 and 0.76 .mu.mol/kg s.c. 8-OH-DPAT in hippocampus than in hypothalamus, striatum and frontal cortex in mentioned order. This order of potency was the opposite to that found for 8-OH-DPAT in decreasing the 5-HTP accumulation. Since previous studies by others have indicated that the reserve of somatodendritic 5-HT1A receptors is greater in dorsal raphe nucleus innervating frontal cortex and striatum than in median raphe nucleus which mainly innervates hippocampus, the obsd. different regional potency of the two 5-HT1A receptor antagonists may be explained by this difference in the 5-HT1A receptor reserve.

ACCESSION NUMBER: 1998:252565 CAPLUS
DOCUMENT NUMBER: 129:49923
TITLE: Differential regional antagonism of 8-OH-DPAT-induced decrease in serotonin synthesis by two 5-HT1A receptor antagonists

AUTHOR(S): Larsson, Lars-Gunnar; Stenfors, Carina; Ross, Svante B.

CORPORATE SOURCE: Preclinical R&D, Biochemical Pharmacology, Astra Arcus, Soedertaelje, Swed.

SOURCE: Eur. J. Pharmacol. (1998), 346(2/3), 209-215
CODEN: EJPHAZ; ISSN: 0014-2999

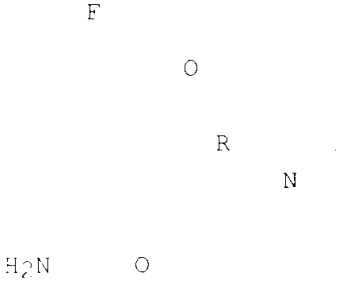
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 9 OF 9 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 1
IT **189311-41-9P 189311-70-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-amino-5-carbamoyldihydrobenzopyrans as 5-HT1A antagonists)
RN 189311-41-9 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(dicyclobutylamino)-8-fluoro-3,4-dihydro-, (R)-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 169758-66-1
CMF C18 H23 F N2 O2
CDES 1:R

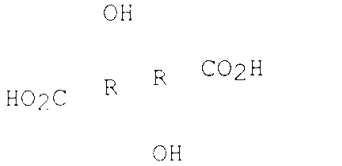
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



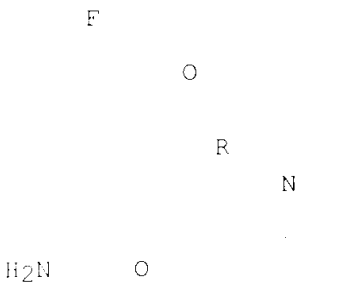
RN 189311-70-4 CAPLUS
CN 2H-1-Benzopyran-5-carboxamide, 3-(cyclobutylcyclopentylamino)-8-fluoro-3,4-

dihydro-, (R)-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 169758-11-2
CMF C19 H25 F N2 O2
CDES 1:R

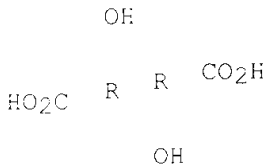
Absolute stereochemistry. Rotation (-).

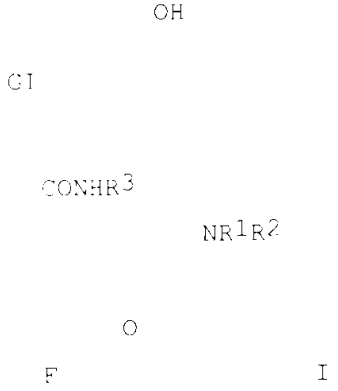


CM 2

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.





AB Title compds. (I; R1 = Pr or cyclobutyl; R2 = CHMe2, CMe3, cyclobutyl, cyclopentyl, cyclohexyl; R3 = H or Me) were prepd. Thus, (R)-3-amino-8-bromo-5-methoxy-3,4-dihydropyran was converted in 9 steps to (R)-I (R1 = Pr, R2 = cyclopentyl, R3 = Me). Data for biol. activity of I were given.

ACCESSION NUMBER: 1997:231466 CAPLUS
DOCUMENT NUMBER: 126:317317
TITLE: Preparation of 3-amino-5-carbamoyldihydrobenzopyrans

as 5-HT1A antagonists

INVENTOR(S): Evenden, John L.; Hammarberg, Eva M.; Hansson, Hans S.; Hellberg, Sven E.; Johansson, Lars G.; Lundkvist, Johan R. M.; Ross, Svante B.; Sohn, Daniel D.; Thorberg, Seth O.

PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.

SOURCE: U.S., 16 pp. Cont.-in-part of U.S. 5,420,151.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5616610	A	19970401	US 1995-362544	19950104
ZA 9207609	A	19930413	ZA 1992-7609	19921002
AU 9227684	A1	19930503	AU 1992-27684	19921008
AU 667687	B2	19960404		
EP 607274	A1	19940727	EP 1992-921525	19921008
EP 607274	B1	19960626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
EP 703229	A2	19960327	EP 1995-118114	19921008
EP 703229	A3	19960626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PL 171013	B1	19970228	PL 1992-303101	19921008
US 5420151	A	19950530	US 1993-144671	19931028
NO 9401256	A	19940407	NO 1994-1256	19940407
FI 9401616	A	19940408	FI 1994-1616	19940408
WO 9511891	A1	19950504	WO 1994-SE1010	19941026
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

SE 1989-4361	19891222
US 1990-633247	19901221
SE 1991-2905	19911008
US 1991-780531	19911018
SE 1992-2000	19920629
US 1992-957214	19921006
US 1993-144671	19931028
WO 1994-SE1010	19941026
EP 1992-921525	19921008
WO 1992-SE708	19921008

OTHER SOURCE(S): MARPAT 126:317317

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FILE 'REGISTRY' ENTERED AT 11:49:00 ON 23 JUL 1999

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L2 2 S L1
L3 STRUCTURE UPLOADED
L4 50 S L3
L5 29 S L1 FUL
L6 8067 S L3 FUL
L7 5 S L5 SUB=L6 FUL

FILE 'CAPLUS, USPATFULL' ENTERED AT 11:54:54 ON 23 JUL 1999
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L8 9 DUP REM L8 (1 DUPLICATE REMOVED)

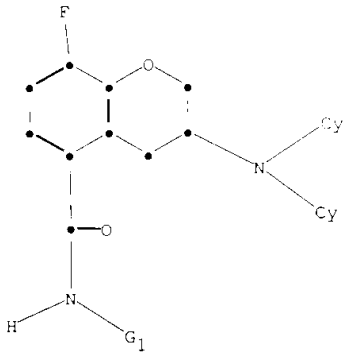
=> log y

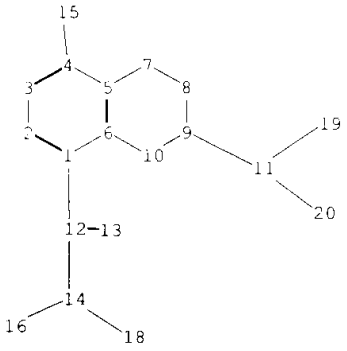
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.42	308.57

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.82	-4.82

STN INTERNATIONAL LOGOFF AT 11:56:50 ON 23 JUL 1999

STN Structure : 9077718.str



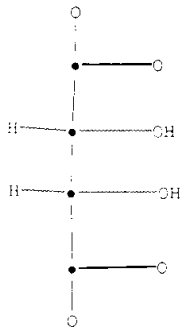


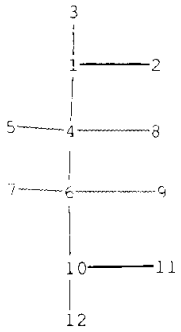
chain nodes :
11 12 13 14 15 16 18 19 20
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-12 4-15 9-11 11-19 11-20 12-13 12-14 14-16 14-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
5-7 6-10 7-8 8-9 9-10 9-11 11-19 11-20 12-13 12-14 14-18
exact bonds :
1-12 4-15 14-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:H,CH3

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS
18:CLASS 19:Atom 20:Atom

STN Structure : 09077718.str





chain nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-2 1-3 1-4 4-5 4-6 4-8 6-7 6-9 6-10 10-11 10-12
exact/norm bonds :
1-2 1-3 4-8 6-9 10-11 10-12
exact bonds :
1-4 4-5 4-6 6-7 6-10

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS 12:CLASS